**Treatment of Patients with Metastatic Melanoma Using Lymphocytes Reactive with the gp100 Antigen Following the Administration of a Nonmyeloablative Lymphocyte Depleting Regimen**

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Non-Technical Abstract:

This study will be performed in patients who have metastatic melanoma. The main purpose of this research study is to determine whether special tumor fighting cells that we take from patients' blood or tumors, grow in the laboratory, select the ones most reactive to the gp100 antigen, and then give back to the patient, will improve the ability to fight the patients' cancer. The cells will be given after we suppress their immune system from attacking these special tumor-fighting cells. In addition, patients will be immunized using a fowlpox vector to deliver a melanoma antigen, gp100:209-217(210M) followed by intravenous high dose interleukin 2 (IL-2). The secondary objective of this study is to determine the survival of these infused cells.

Initially patients will have lymphocytes harvested either through leukopheresis and/or a biopsy of their tumor. The lymphocytes will be grown in the laboratory. Up to 29 patients will be treated with lymphocytes harvested from a tumor, and up to 29 patients will receive lymphocytes harvested through leukopheresis.

Once the cells are grown in the laboratory, patients will be given chemotherapy, (cyclophosphamide and fludarabine) for seven days to suppress the immune system. On the eighth day, they will be given intravenous fowlpox virus rF-gp100P209 over 1-2 minutes, followed by the cells intravenously over 20-30 minutes, followed within 24 hours by intravenous Interleukin 2 (IL-2, a hormone that stimulates lymphocyte growth) at 720,000 IU/kg every 8 hours for up to 15 doses, depending on patient tolerance. Patients return on day 28 to receive a second intravenous infusion of fowlpox virus rF-gp100P209 followed by a second cycle of IL-2. Patients will be given appropriate medications to treat the side effects of this treatment regimen and to prevent infection secondary to the immune suppression caused by the chemotherapy.

Patients will return to NIH four to six weeks after cell infusion to have their tumor(s) evaluated. If there is shrinkage of their tumor(s), the cell infusion will be repeated. If there is no response, patients may be offered treatment with cells administered in an artery (intra-arterial, i.a.) supplying the tumor if the tumor location and blood supply is appropriate. Patients who do not have tumors/blood supply amenable to i.a. administration and develop progressive disease after i.v. cell infusion will be taken off this study. Patients whose tumors grow after receiving cells by the i.a. route will be taken off study. In patients who are responding, up to two retreatment courses may be given.